Abstract

Introduction

Adolescents, relative to adults, show impairments in learning to reduce or *extinguish* fear. Furthermore, they may struggle with the use of reappraisal techniques to regulate affect. Both learning and reappraisals are critical to cognitive-behavioural treatments (CBT) for anxiety disorders leading to the hypothesis that adolescents may respond more poorly to CBT than adults.

Methods

We use meta-regression to explore whether variability in the mean age of participants in trials of CBT for anxiety predicted variability between studies in symptom change effect sizes. PsycARTICLES, PsycINFO, MEDLINE and Embase databases were searched with the terms *exposure* and each of *anxiety*, *phobia*, or *panic disorder* diagnostic terms and *cognitive behav* therapy* with each of the diagnostic terms. Data were pooled from CBT trials for anxiety disorders (excluding anxiety-related disorders – obsessive compulsive disorder and posttraumatic stress disorder) where participants' mean age was 11 years or older.
149 studies were selected and data on change in symptoms from pre-treatment to post-treatment (k = 195), pre-treatment to follow-up (k = 108) and post-treatment to follow-up (k = 107) were extracted.

Results

Several possible confounding variables were also accounted for (e.g., proportion of females, number of sessions). Younger age was associated with smaller improvement in anxious symptoms from pre- to post-treatment. However, younger age was also associated with greater improvement in symptoms from post-treatment to follow-up.

Conclusions

CBT is effective at reducing anxious symptoms, however, younger people may respond more slowly to treatment than older people.

Keywords: Anxiety; Phobia; Adolescence; Exposure; Cognitive-Behavioural Treatment

Introduction

Anxiety disorders pose considerable distress, disability and cost to individuals and economies worldwide (Baxter, Scott, Vos, & Whiteford, 2013; Baxter, Vos, Scott, Ferrari, & Whiteford, 2014). Many cases of anxiety begin in youth (Kessler, et al., 2005), posing significant long-term academic and social disadvantage (Van Ameringen, Mancini, & Farvolden, 2003). Young people with diagnoses of anxiety disorders such as specific phobia, social anxiety disorder, panic disorder and generalised anxiety disorder, are also at elevated risk of subsequent substance abuse and mood disorders in adulthood (Pine, Cohen, Gurley, Brook, & Ma, 1998). The gold-standard treatment for anxiety disorders – Cognitive Behavioural Therapy (CBT) – is highly efficacious in ameliorating anxiety symptoms (Bennett, et al., 2013; Berlim, Van den Eynde, & Jeff Daskalakis, 2013; Chorpita, et al., 2011; Drysdale, et al., 2014; Hofmann & Smits, 2008; Kendall & Peterman, 2015). However, 40-50% of people will not respond to treatment (Walkup, et al., 2008) and, among those who do, up to 62% will experience a return of fear later (Craske & Mystkowski, 2006). For adolescents, they may be more likely than adults to show problems with the kind of learning and techniques that are thought to be critical to CBT for anxiety disorders, such as with *extinction learning* (Baker, Den, Graham, & Richardson, 2014) or in applying reappraisal techniques to regulate negative affect (McRae et al., 2012; Silver et al., 2012). Because of these age-typical differences, adolescents with anxiety may respond more poorly to CBT than anxious adults. Although there is a wealth of evidence from CBT studies involving either adolescents or adults with anxiety disorders, this research has yet to be combined meta-analytically to examine whether, across all existing studies, there are important age-related differences in CBT outcomes. The present study will provide the first such analysis with a view to informing our understanding of whether adolescents perform less well in CBT than adults.

CBT involves multiple treatment components such as psychoeducation, cognitive restructuring or reappraisal training and behavioural exposure. During the exposure component of CBT people are repeatedly exposed to the object of their fears. Extant research in this area suggests that exposure is perhaps the most important aspect of CBT (Wolitzky-Taylor, Horowitz, Powers, & Telch, 2008) and as such it is often delivered in a standalone format without the other components in adults and young people (Wolitzky-Taylor et al., 2008; Chorpita, et al., 2011). Contemporary theories regarding exposure suggest that fear reduces or *extinguishes* as a person learns that a stimulus or situation that they fear (e.g., when their heart rate is perceived to be faster than usual in the case of panic disorder) is no longer predictive of the aversive outcome they expected would follow this stimulus/situation (e.g., that this pattern of heart activity is not predictive of an impending heart attack) (Bouton, 2004; Vervliet, Baeyens, Van den Bergh, & Hermans, 2013). In experimental models of extinction learning healthy adolescents (aged 10-17 years) have shown evidence of impairments such that their fear for discrete stimuli does not reduce across time (Haddad, Lissek, Pine, & Lau, 2011; Lau, et al., 2008) and when compared to adults (Britton, et al., 2013; Pattwell, et al., 2012). Furthermore, adolescents' fear may be more likely than adults' to return after it has been extinguished, again suggesting that the initial extinction learning was impaired (Britton, et al., 2013; Den, Graham, Newall, and Richardson, 2015). Similar age-related impairments in extinction learning have also been found in studies with juvenile rodents (Baker, Bisby, & Richardson, 2016; Baker & Richardson, 2015). It is also of note that amongst children and adolescents, poor extinction abilities measured prior to treatment have been associated with worse treatment responses (Waters & Pine, 2016).

Cognitive reappraisal, another component of CBT, refers to the use of more effortful strategies to reinterpret an emotion-eliciting stimulus or situation to alter its meaning and

change its emotional impact. While this appears to be a promising way to regulate negative affect in adults, the adolescent capacity to deploy these strategies may be modulated by structural immaturity of neural circuits involved in top-down inhibition of affective responses. Experimental studies comparing cognitive reappraisal abilities in children, adolescents and adults have shown linear but also quadratic relations between age and regulation success. Put otherwise, the ability to effectively down-regulate emotions evoked by negative stimuli, using behavioural but also neural indices of affect, develops throughout adolescence and into adulthood (McRae et al., 2012; Silvers et al., 2012).

Given the comparative difficulty with extinction learning and cognitive reappraisal ability that adolescents show relative to adults, and the importance of this learning in CBT for anxiety disorders, we might infer from this that anxious adolescents may show greater difficulty in responding to treatment compared with adults. It must be noted that although adolescents and adults differ in many of these comparisons when considered categorically, adolescence is a dynamic stage of life where there is tremendous biological, psychological and social change. In particular, during adolescence prefrontal brain regions known to be important in the management of fear and anxiety undergo significant maturation (Caballero, Granberg & Tseng, 2016). As such, we might expect there to be continuous change across adolescence into adulthood in responsiveness to CBT. Such age-related differences in treatment responses would contrast with the intuitive presumption that anxiety disorders would be more easily treated at earlier ages because these disorders had presumably emerged not long before treatment. This is relative to anxiety disorders that are treated in adulthood that might have emerged much earlier in life. Although some meta-analytical research has already compared CBT outcomes between children and adolescents, with no evidence of a difference between these age groups in CBT effectiveness (Bennett, et al., 2013; Drysdale, et al., 2014; Kendall & Peterman, 2015), no meta-analyses of the effects of

age in the adolescent-to-adult age range have been conducted. It is important that such an analysis takes a continuous approach to age given the change that takes place across adolescence. Our findings might support the need for further adoption of extinction-enhancing techniques (see Craske, Treanor, Conway, Zbozinek, & Vervliet, 2014) or more targeted strategies to encourage the use of cognitive reappraisal in treatments involving adolescents.

Meta-regression techniques were used to examine whether the mean age of participants within a study group predicted differences between studies in the extent to which symptoms changed across and following treatment. We hypothesised that across analyses of symptom change from pre-treatment to post-treatment and pre-treatment to follow-up, the age of participants would show a positive association with study effect sizes. We expected that smaller effects, or less *decrease* in symptoms from pre-treatment, would be associated with younger age. Also, given the evidence that adolescents may be more likely to show a return of fear after extinction than adults, we also hypothesised that age would show a negative association with study effect sizes in our analysis of change in symptoms from post-treatment to follow-up. Put otherwise, we expected that younger age would be associated with greater *increase* in symptoms after treatment.

To capture continuous age effects across adolescence and adulthood, we defined the lower age limit as 11 years in line with previous studies in this area (e.g., Bennett et al., 2013). This age limit allowed us to exclude child samples where CBT is often delivered with parental input, concurrent treatments for other family members or without exposure. Also, this age represents the transition to independence that characterises adolescence as young people enter secondary education. Similarly, we defined the upper age limit of our adult sample as 60 years to remove any confounds of age-associated cognitive decline with responsiveness to CBT treatments (Evans, 2007).

As our hypotheses partly related to the extinction mechanisms underlying the exposure component of CBT, it was important that any trials without this component or where parental factors might moderate any treatment effects were excluded. Given our particular interest in the exposure component of CBT we examined if there were differential effects on symptom change for trials involving exposure-alone versus CBT that includes exposure as well as other components such as cognitive reappraisal training. We considered potential covariates regarding sample characteristics, notably, whether there were effects of gender on symptom change. We also accounted for the number of treatment sessions and if the trial involved individual- or group- delivered treatment. However, we had no specific hypotheses regarding the presence of or direction of any possible effects of these variables.

Method

Search strategy

Relevant studies were identified through a systematic search of four databases: PsycARTICLES, PsycINFO, MEDLINE and Embase, selecting all relevant articles from the earliest date for each journal within these databases until 21 October 2015 when the first search was completed. Due to the lengthy time taken for data extraction and analysis, an additional search was completed on 9 October 2017 to account for any additional publications. In total six database searchers were conducted: three searches with the term *exposure* and each of three diagnostic terms - *anxiety*, *phobia*, or *panic disorder* – and, then *cognitive behav* therapy* in combination with each of the three diagnostic terms. After this initial search, duplicates were removed and the titles and abstracts of studies were read for conformity to study selection criteria. Additional articles were included where they had been cited within selected articles but where our initial search had missed them.

Study selection

Included studies involved CBT or exposure therapy alone involving participants older than 11 years of age and younger than 60 years with a primary diagnosis of an anxiety disorder, who had not already been marked as treatment resistant and whose treatment was focused on a primary diagnosis and not some other comorbid disorder. Studies involving CBT were inspected to ensure that the treatment delivered in this study included an exposure component. Also, groups within studies that received any other technique for augmenting treatment were excluded (e.g., attention modification or pharmaceutical agents), but groups that received exposure or CBT in combination with a placebo were included. Treatments did not necessarily have to be delivered in-person by a clinician but exposures had to be clinician-supervised to ensure that they were adhered to fully, as our main study hypotheses involved the effects of age on learning during exposure. Studies involving imaginal or virtual reality exposure, as well as the more typical in vivo exposure, were included. Single case studies or studies using participants with sub-threshold symptom severity were excluded. Studies were excluded if they involved treatment of disorders in other family members (e.g., the treatment of parents' anxiety). Studies where treatment also focused on response prevention or solely on imaginal exposure, and studies which involved anxiety-related disorders such as in Obsessive-Compulsive Disorder (OCD) and Post-traumatic Stress Disorder (PTSD), were excluded from the present analysis. See Figure 1 for a flow chart of the search and study identification process. 2710 studies were identified in the initial search and, after exclusion, 149 studies remained, within which there were 195 effect sizes for pre-treatment to post-treatment (N = 8144), 108 effect sizes for pre-treatment to follow-up (N = 3780) and 107 effect sizes for post-treatment to follow-up (N = 3728) comparisons.

Data extraction

The following data were extracted from each article by T.J.B. and S.P.Y.: 1) author(s) name; 2) year of publication; 3) sample size at pre-treatment, post-treatment and follow-up;

4) mean age of the sample; 5) data regarding the primary diagnosis of the sample (e.g., specific phobia, social anxiety disorder, panic disorder, generalised anxiety disorder or 'mixed' where the trial involved participants with a range of anxiety diagnoses); and, 6) mean score and standard deviation for the primary outcome measure at pre-treatment, post-treatment and follow-up. Where several primary outcomes were included in a study, clinician-rated measures (e.g., scores from clinical interviews) were extracted if they were available, otherwise self-rated measures (e.g., questionnaires) were extracted. These measures took priority over other kinds of measure such as Behavioural Avoidance Tests (BATs) as these behavioural measures were far less common within the literature. Regarding follow-up data, where a study had several follow-up assessments, data from the assessment most distant in time from post-treatment were extracted.

Data regarding potential covariates were also extracted: 1) percentage of female participants; 2) number of treatment sessions; 3) whether the trial was individual or group treatment (coded as 0 and 1 respectively); 4) whether the trial involved exposure alone or exposure as part of a larger CBT program (coded as 0 and 1 respectively). Our index of the number of treatment sessions did not code for differences in session duration as few studies were explicit about the length of each individual session.

Data handling and analysis

The metan and metareg packages of STATA 14.2 were used for analyses. Data were analysed using a random effects framework that assumes that the effect of treatment on anxious symptoms varies between studies. This enables greater generalisation from the studies analysed here to other studies within the field. Pooled standard mean differences (*d*) were computed using Cohen's method. Between study heterogeneity was estimated using the DerSimonian and Laird method and tau-squared (τ^2) served as the index of between study heterogeneity (Borenstein, Higgins, Hedges, & Rothstein, 2017). Thus, standard mean

differences and 95% confidence intervals (CI) were given for each effect size with adolescent and adult samples, for each time point of interest: change from pre-treatment to post-treatment, change from pre-treatment to follow-up and change from post-treatment to follow-up. The significance of these pooled *d*s was calculated using a *Z* test. To reduce the effect of outliers on our analyses, within each time point, effect sizes that were 3 or more standard deviations greater than or less than the mean effect size for that time point were excluded from analyses. Four effect sizes were excluded from pre- to post- treatment analysis (Beidel et al., 2014; Soravia et al., 2014; Spence et al., 2017; Spence et al., 2011). Three effect sizes were excluded from pre- to follow-up analysis (Marks et al., 1993; Spence et al., 2011; Spence et al., 2017). Two effect sizes were excluded from post- to follow-up analysis (Spence et al., 2011; Spence et al., 2017).

We first present the overall size of the effect for change in symptoms for each of the time points across age groups, and an estimation of the amount of variance between studies in the size of the effect sizes. Where there was evidence of significant variance in the size of effects, for descriptive purposes we then present a categorical meta-analysis of each age group separately. This was followed up by random effects meta-regression to explore age as a continuous predictor of symptom change for each of the time points. Where there was evidence of a significant linear relationship between age and symptom change, additional potential confounds were entered into the meta-regression to explore whether the variance in treatment change that was explained by age was independent of these confounds (e.g., proportion of females, the number of treatment sessions, whether the trial was mere exposure or exposure within a larger CBT package and whether treatment was delivered at an individual or group level). The independent effects of each of the included variables with the meta-regressions was calculated using a *Z* test.

We then explored whether there was evidence of publication bias, first by visually inspecting funnel plots and then statistically using Egger's test to assess whether effect sizes were related to sample sizes. Vevea and Woods' (2005) sensitivity analysis was then performed, which adjusts pooled effect sizes based on the presence of moderate and severe one- and two-tailed selection biases. The absence of publication bias in this test is evidenced by similarity in these adjusted and unadjusted effect sizes.

Results

Sample-wide, adolescent and adult group sample characteristics are displayed in Table 1. A full list of references of included studies and forest plots of effect sizes is available in the supplemental materials.

Pre- to post- treatment

Across both age groups, there was a large effect of treatment on change in anxiety symptoms (d = 1.302, CI[1.203, 1.401], Z = 25.79, p < .001). There was also a substantial amount of variance between studies in the size of the change in symptoms from pre- to post-treatment (τ^2 = .392, $\chi^2(194)$ = 1424.78, p < .001). Separating adolescents (>11 years of age and < 19 years of age) from adults (>/=19 years) categorically for descriptive/interpretative purposes, both adults (d = 1.321, CI[1.214, 1.427], Z = 24.22, p < .001) and adolescents (d = 1.189, CI[.924, 1.453], Z = 8.81, p < .001) showed significant change in symptoms from pre- to post- treatment.

In a meta-regression including mean age for each effect size as a predictor variable, and the effect size for change from pre- to post- treatment as the dependent variable, age explained a trend-level amount of variance in symptom change effect sizes (B = .012, SE = .006, Z = 1.91, p = .056). The effect of age became significant when the additional potential confounds were included in the model (B = .013, SE = .007, Z = 1.97, p = .049). Of these other variables, only the proportion of females explained a significant amount of variance in

study effect sizes (B = .008, SE = .004, Z = 2.15, p = .032) (See Table 2 for full description of meta-regression findings). This model explained 3.7% of the variance in effect sizes for symptom change. Older age was associated with greater decrease in symptoms from pre- to post-treatment, however, the amount of between-study variance in symptom change that was explained by participants' age was small. Studies that had a higher proportion of females also showed greater decrease in symptoms.

Pre-treatment to follow-up

Overall there was a large effect of treatment on change in anxious symptoms from pre-treatment to follow-up (d = 1.457, CI[1.314, 1.599], Z = 20.06, p < .001) with substantial variance between studies in the size of this effect (τ^2 = .449, $\chi^2(107)$ = 772.86, p < .001). Separating the groups categorically, effect sizes for change in symptoms from pre-treatment to follow-up assessment were similar for adults (d = 1.435, CI[1.275, 1.595], Z = 17.56, p < .001) and adolescents (d = 1.562, CI[1.272, 1.853], Z = 10.54, p < .001).

In a meta-regression, age was not a significant predictor of change in symptoms from pre-treatment to follow-up (B = .001, SE = .007, Z = .17, p = .863).

Post-treatment to follow-up

Across the age groups there was evidence of a significant reduction in symptoms from the end of treatment to follow-up assessment such that symptoms continued to decrease after treatment (d = .213, CI[.148, .279], Z = 6.37, p < .001). There was also a significant amount of variance between studies in the size of this decrease (τ^2 = .045, $\chi^2(106)$ = 190.14, p < .001). Both age groups showed positive pooled effect sizes such that symptoms continued to decrease from the end of treatment to follow-up with adolescents showing somewhat more change (d = .307, CI[.214, .401], Z = 6.44, p < .001) than adults (d = .190, CI[.112, .269], Z = 4.77, p < .001).

In a meta-regression age explained a significant amount of variance in between-study differences in effect sizes for symptom change from post-treatment to follow-up assessment (B = -.007, SE = .003, Z = -2.19, p = .028). When the potential confounds were entered into the model, age continued to explain a significant amount of variance in between-study differences in symptom change (B = -.007, SE = .003, Z = -2.28, p = .023). The only confound which explained a significant amount of variance in effect sizes was if treatment was delivered as exposure alone or a full package of CBT (B = .239, SE = .118, Z = 2.03, p = .042). The direction of this effect was such that studies involving a full package of CBT were associated with greater decrease in symptoms from post-treatment to follow-up, compared with if exposure was delivered on its own. None of the other potential confounds explained a significant amount of variance in symptom change (p > .05) (See Table 2). This model explained 20.1% of the variance in symptom change. Studies with older participants showed less change in symptom severity from post-treatment to follow-up assessment than studies with anxious people who were younger.

Publication bias

Funnel plots of effect sizes for each of the analysis time points against standard errors for these effects suggested that there was evidence of a publication bias in the data for pre-treatment to post-treatment symptom change (see Figure 2 for funnel plots). This was confirmed by Egger's test, t(194) = 3.28, p = .001. However, Vevea and Woods (2005) adjusted effect sizes accounting for severe two-tailed bias were similar to the unadjusted effect sizes across age-groups, suggesting that if we were to account for this publication bias in our analysis this would not have had a marked influence on our analyses (adjusted d = 1.276). Egger's test for the other time points suggested that there was no evidence of a bias in the pre-treatment to follow-up, t(107) = .52, p = .605, or post-treatment to follow-up data, t(106) = -.55, p = .585. Again, Vevea and Woods (2005) adjusted effect sizes accounting for

severe two-tailed bias were similar to the unadjusted effect sizes for overall symptom change across age-groups (pre-treatment to follow-up adjusted d = 1.390; post-treatment to follow-up adjusted d = .131)

Discussion

Adolescents relative to adults have been found to show difficulties in the extinction of fear (Baker, et al., 2014) and in reappraisal of negative affect (McRae et al., 2012; Silvers et al., 2012). These aspects of behavioural and cognitive emotion regulation are critical components of CBT for anxiety disorders (Craske, et al., 2008). This meta-analysis provided the first, and most comprehensive, examination of whether the age of adolescent and adult participants in trials of CBT would explain differences in treatment effect sizes. Combining the findings from each of the analyses performed here, there was evidence that older age was associated with greater reduction in symptoms from pre-treatment to post-treatment, but not symptom change from pre-treatment to follow-up. Also, younger age was associated with greater reduction in symptoms from post-treatment to follow-up. It must be noted, however, that age explained only a small amount of the heterogeneity in effect sizes between studies in our pre- to post- treatment analysis. There was also evidence that while older people may have responded better to CBT by post-treatment, younger people's symptoms continued to decrease after post-treatment such that there was no difference between age-groups in their symptoms by follow-up assessment. Despite the observed effect of age on symptom change, it is worth underscoring that both age groups, when separated categorically, showed substantial treatment effects. Clearly, CBT for anxiety disorders is highly effective in reducing symptoms.

Our study sampled the totality of existing evidence regarding CBT for anxiety disorders across adolescence and adulthood. Our results from pre-treatment to post-treatment but not from pre-treatment to follow-up could be attributed to the suggestion that adolescents

show *slowed* extinction relative to adults (Britton, et al., 2013). Adolescents may take longer to consolidate the learning that takes place in treatment. It could also be that adolescents need more practice before they are competent with using reappraisal strategies and may also receive additional support from their families in these coping styles following treatment to the benefit of their anxious symptoms. Research must now examine what factors explain this continued improvement in symptoms, outside of treatment amongst adolescents. Another interpretation could be that older participants merely had increased symptom severity at pre-treatment compared with younger participants so they showed a sharper decline in symptoms by post-treatment. However, if this was the case we would either expect the same age-related trend in our post-treatment to follow-up analysis as older participants' symptoms continued to reduce or we would expect no age effect if younger participants had such low symptom severity that their symptoms could not further decrease during or after treatment.

Our findings contrast with the intuitive expectation that responsiveness to treatment would be best in adolescence because the time of disorder onset is presumably nearer to treatment than would be the case for adults. As disorder onset time is rarely, if ever, quantified, we were unable to provide a definitive examination of this question. It would be interesting to examine whether disorder onset time moderates any of the observed effects. It must be noted that although our hypotheses were derived from evidence suggesting that adolescents show an impairment in extinction learning and reappraisal ability relative to adults, we did not examine whether age-related differences in these behavioural and cognitive aspects of emotion regulation directly explained age-related differences in treatment responses. It is possible that adolescents and adults may differ in their initial responsiveness to CBT for other reasons such as age-related differences in social or therapeutic processes such as a failure to align treatment to the desire for autonomy in adolescents or, more broadly, to use developmentally appropriate language and treatment

materials that are sensitive to adolescent norms (Kendall & Peterman, 2015). Future research must quantify these other possible factors as well as extinction and reappraisal problems in examining age-related differences in treatment responses.

It is important to note that age only explained a small amount of variance in treatment effect sizes from pre- to post- treatment. Neither adolescents nor adults are homogenous groups of people and there are multiple factors that might explain differences in treatment responses between individuals besides their age. Such intra-age-group variability is perhaps particularly prominent in adolescence where there is substantial biological, psychological and social change. In order to examine the processes that influence treatment responsiveness amongst adolescents, research must now examine whether variability in these characteristics, perhaps in the underlying neurobiology of fear and anxiety (Milad & Quirk, 2012; Vervliet et al., 2013), explains additional variance in treatment responsiveness. It is also of note that although we found evidence of publication bias within the analysis of symptom change from pre-treatment to post-treatment, our sensitivity analysis showed that the inclusion of unpublished data would be unlikely to change the overall findings for symptom change across adults and adolescents.

Two other findings emerged from our analysis of potential covariates. First, that studies with a higher proportion of females showed greater decreases in symptoms from pre-treatment to post-treatment and second, that studies involving a full package of CBT were associated with greater decrease in symptoms from post-treatment to follow-up relative to studies involving exposure alone. The gender effect might be explained by differences in the therapeutic relationship between males and females (Bhati, 2014; Wintersteen, Mensinger & Diamond, 2005), with females responding more strongly to the therapeutic environment than males, and so responding more rapidly to treatment. Nevertheless, given that there were no

gender effects by follow-up it seems that both genders are equally likely to respond well to treatment over the longer term.

The finding that CBT was associated with greater decrease in severity from post-treatment to follow-up versus exposure alone is not entirely clear given that this variable was not associated with symptom change from pre-treatment to post-treatment or pre-treatment to follow-up. These findings suggest that neither treatment form is better than the other at modifying symptom trajectories from pre-treatment. It could be that some other component of CBT besides exposure might exert change on symptoms in a delayed manner following treatment cessation. However, future research must clarify this point in comparisons of CBT and exposure alone with mediational analyses during follow-up periods.

Although the effect of age observed here were small, we might nonetheless offer some recommendations to clinicians to enhance treatment responsiveness. Given the suggestion that adolescents may respond less well to CBT initially, clinicians might adopt techniques already more common in the treatment of adult anxiety for enhancing treatment learning (Craske et al., 2014). For example, clinicians could ensure that greater attention is given to establishing what it is an anxious adolescent expects when they are in the presence of a feared stimulus and then focus on violating this expectancy. They might also vary stimuli and situations as much as possible within treatment and present as many of them as possible, concurrently where possible, whilst removing safety behaviours, encouraging clients to label their emotional experiences and ensuring that attention stays maintained on feared stimuli during exposure. Although these practices may already be utilised by *some* clinicians, it remains unclear whether the most evidence-based approaches are being utilised fully by clinicians (Chorpita et al., 2011) and whether this includes exposure with an emphasis on enhancing extinction learning (Wolitzky-Taylor, Zimmermann, Arch, De Guzman & Lagomasino, 2015). In terms of reappraisal techniques, there are also

experimental interventions designed to encourage the re-interpretation of negative stimuli to a more benign focus. As an example, cognitive bias modification techniques, while currently yielding weak effects in single-session studies (Krebs et al., 2018), could be optimised across multiple sessions with more engaging stimuli to reduce anxiety (Lisk et al., 2018). Functional MRI based neurofeedback to enhance cognitive reappraisals also shows promise particularly if one of the reasons for difficulties is the immaturity of prefrontal inhibition of affective responses in subcortical regions (Cohen Kadosh et al., 2016). As such, if adolescents are more likely to respond more slowly to treatment than adults then greater emphasis should be placed on establishing whether these experimental techniques could enhance extinction learning and cognitive reappraisals.

Limitations

It is notable how few groups of data there were for adolescents compared with adults. For this reason, we were relatively liberal in our inclusion criteria of selecting studies where the mean age was 11 years. However, a downside of this was that younger children were also included in the meta-analysis given that a sample where the mean age is 11 is likely to include pre-adolescent children. This seems unavoidable given that, as reported elsewhere (Kendall & Peterman, 2015), many trials in this area have liberal criteria for what constitutes adolescence and as such often involve younger children as well. Many of these studies also often involve mixed samples of several different diagnostic groups. We were unable to identify any studies within our inclusion/exclusion criteria involving adolescent participants where treatment was specifically for Panic Disorder or Generalised Anxiety Disorder, although these disorders were included in some of the mixed-diagnosis studies that were included (Nauta, Scholing, Emmelkamp, & Minderaa, 2003; Shechner, et al., 2014). The level of heterogeneity that is expected amongst these age groups and between diagnoses made it difficult to fully and robustly examine the effects of CBT and exposure on anxiety

symptoms within adolescence or to explore disorder specific effects. It is also possible that adolescents were more likely to be medication naïve than adults given that adolescents were unlikely to have been diagnosed as anxious for as long as adults. However, medication use was not consistently reported across the studies that were sampled. This prevented us from exploring whether differences in the use of medication between adolescent and adult samples had any influence on the observed effects.

In our analysis of follow-up data, we extracted data from the latest follow-up time point within each study. This time point varied across studies, and although it would be possible to analyse whether the length of time between post-treatment assessments and the last follow-up assessment further predicted effect sizes, and perhaps also interacted with age, these data were not extracted in the current study because there were no a priori hypotheses regarding this variable prior to our analysis. Future research, perhaps building on the data set presented here, could extract these data and examine these effects.

Regarding the number of treatment sessions recorded in our analysis, studies either reported the total number of treatment sessions within a given study or the average number of treatment sessions that the participants in their study completed. This inconsistency between studies means that we could not definitively control for possible age-related differences in the number of treatment sessions completed and the potential effect of this on treatment responses. Also, there was inconsistency between studies regarding the length of time of a given session – some studies included fewer sessions but delivered treatment in a massed format across several hours.

Conclusion

We provide the first meta-analysis of age-related differences in treatment responses for anxiety disorders in adolescents and adults. Our highly comprehensive meta-analysis and meta-regression offers the strongest support yet for the suggestion that CBT and exposure

therapy are associated with large changes in anxiety severity but that younger people may respond more slowly to treatment than older people. Despite this finding, there is a relative lack of treatment trials in adolescence and even fewer studies examining ways in which treatment might be improved for this age group. By taking the broadest possible view of existing evidence in this area it has also become clear that there is a pressing need for greater quantity of research regarding the treatment of adolescent anxiety. In particular, there is a need for further examinations of the factors which moderate treatment within this group, perhaps in terms of individual differences in fear learning and extinction processes, cognitive reappraisal techniques or other therapeutic or social processes.

Table 1. Study characteristics

	Pre-treatment to post-treatment			Pre-treatment to follow-up			Post-treatment to follow-up		
	Total	Adol.	Adults	Total	Adol.	Adults	Total	Adol.	Adults
N	8144	1125	7019	3780	871	2909	3728	871	2857
k	195	26	169	108	19	89	107	19	88
Age	30.97	12.93	33.74	29.76	13.28	33.27	29.71	13.28	33.25
	(9.25)	(2.55)	(6.30)	(9.91)	(2.81)	(6.84)	(9.95)	(2.81)	(6.87)
Females	64.0%	55.7%	65.3%	66.8%	59.3%	68.4%	66.8%	59.3%	68.4%
Prop.									
Mixed	13.3%	53.8%	7.1%	12.0%	42.1%	5.6%	12.1%	42.1%	5.7%
SAD	34.9%	19.2%	37.3%	34.3%	26.3%	36.0%	32.7%	26.3%	34.1%
Specific	20.0%	26.9%	18.9%	26.9%	31.6%	25.8%	27.1%	31.6%	26.1%
Panic	26.2%	0.0%	30.2%	20.4%	0.0%	24.7%	21.5%	0.0%	26.1%
GAD	5.6%	0.0%	6.5%	6.5%	0.0%	7.9%	6.5%	0.0%	8.0%

Sessions	8.64	9.16	8.56	8.32	7.56	8.47	8.25	7.56	8.40
	(5.19)	(5.48)	(5.15)	(5.55)	(4.84)	(5.69)	(5.54)	(4.84)	(5.70)
Prop. CBT	68.7%	76.9%	67.5%	64.8%	68.4%	64.0%	63.6%	68.4%	62.5%
Prop. Group	36.9%	34.6%	37.3%	33.3%	42.1%	31.5%	32.7%	42.1%	30.7%

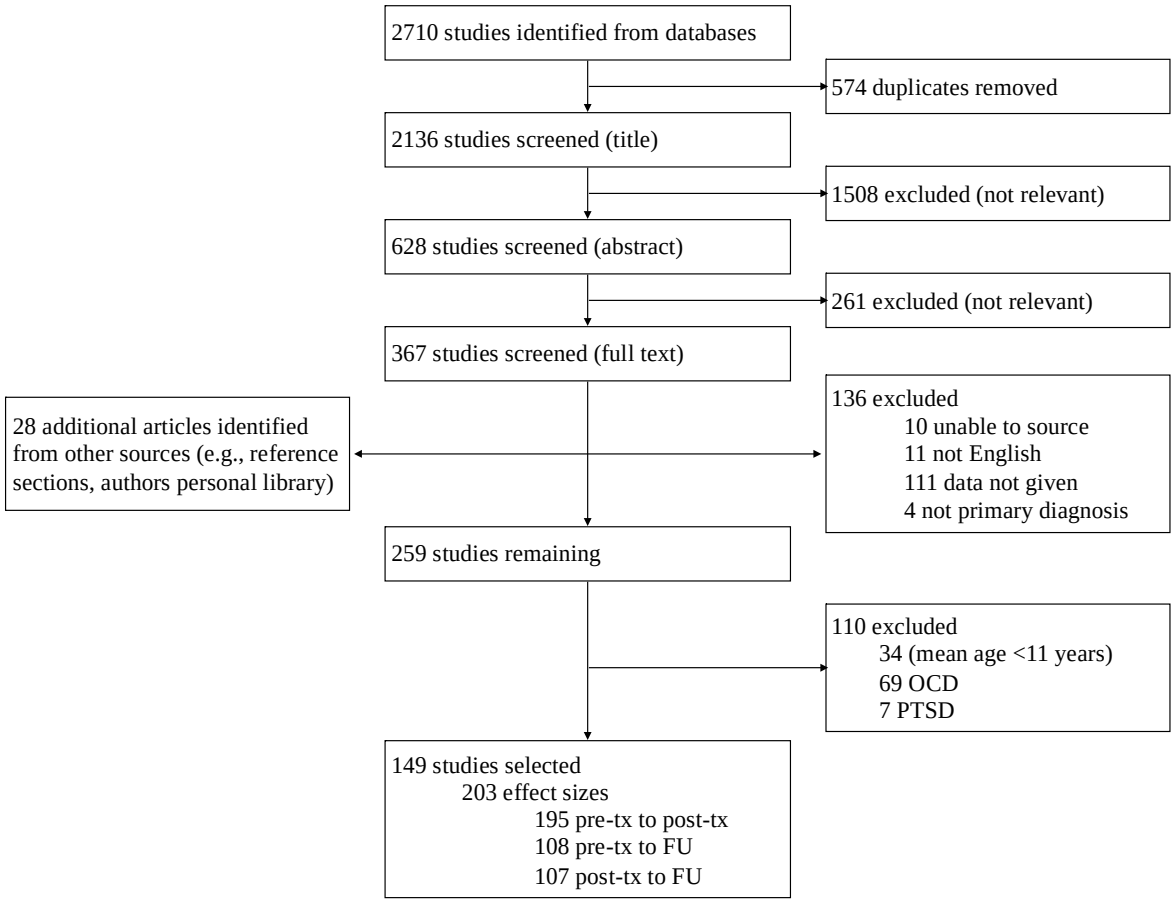
Note. Total sample characteristics. Data are given for effect sizes with a mean age greater than 11 years and less than 19 years (Adol.: adolescents) and for effect sizes with a mean age greater than 19 (adults). Where means are given, standard deviations are presented in parentheses. Prop. Diagnoses refers to the proportion of effect sizes for each diagnostic category within a given age category. Sessions refers to the average number of treatment sessions. Prop. CBT refers to the proportion of effect sizes involving cognitive behavioural therapy, where the remaining effect sizes would be exposure alone. Prop. Group refers to the proportion of effect sizes involving group therapy, where the remaining percentage would be individual therapy Mixed: Studies with participants from several diagnostic groups; SAD: Social Anxiety Disorder; Specific: Specific Phobia; Panic: Panic Disorder; GAD: Generalized Anxiety Disorder.

Table 2. Meta-regression

	Pre-tx to post-tx			Post-tx to follow-up		
	Beta	*SE*	*Z*	*Beta*	*SE*	*Z*
Step 1						
Age	.012	.006	1.91^{+}	-.007	.003	-2.19*
Step 2						
Age	.013	.007	1.97*	-.007	.003	-2.28*
Gender	.008	.004	2.15*	.002	.002	1.29
Sessions	-.008	.016	-.51	-.008	.010	-.083
Exp. or CBT	-.090	.185	-.49	.239	.118	2.03*
Individual or Group	.177	.138	1.28	-.125	.072	-1.73

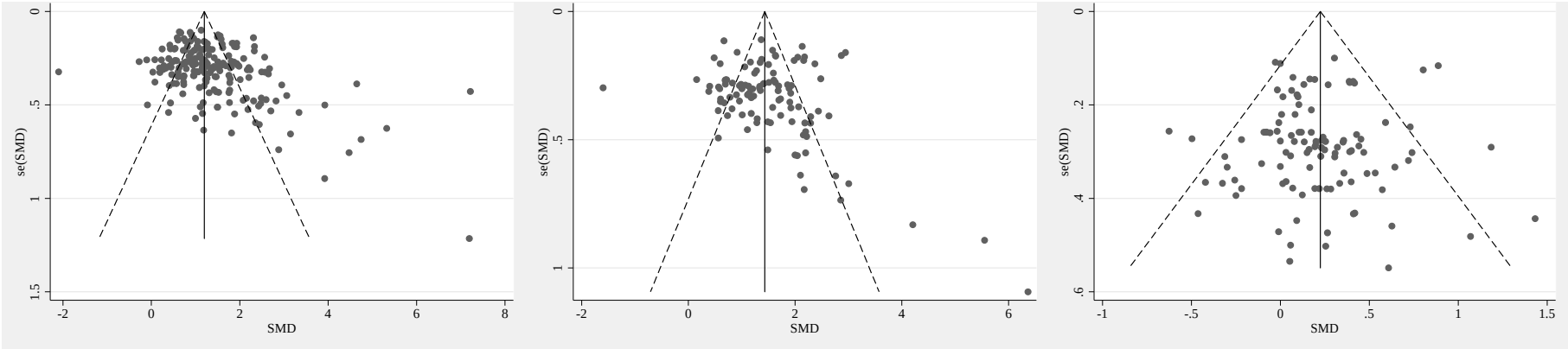
Note. Meta-regression predicting change in symptoms from pre-treatment (pre-tx) to post-treatment (post-tx) and from post-treatment to follow-up assessments, where mean age is entered in the first step and potential confounds are added in the second step. Results are not presented for our analysis of pre-treatment to follow-up symptom change as age was not a significant predictor in the first step of that meta-regression. Gender refers to the proportion of females. Sessions refers to the average number of treatment sessions. Exp. or CBT refers to whether or not treatment was exposure therapy alone or cognitive behavioural therapy. Individual or group refers to whether or not the treatment was delivered in an individual or group format. $^{+}$: $p = .06$; *:$p < .05$.

Figure 1. Study search and inclusion/exclusion



Note. Flow chart of article inclusion and exclusion. OCD: Obsessive Compulsive Disorder; PTSD: Post-traumatic Stress Disorder; pre-tx: pre-treatment; post-tx: post-treatment; FU: Follow-up.

Figure 2. Funnel plots



Note. Funnels plots of effect sizes (SMD: Standard Mean Difference (Cohen's *d*)) for symptom change for the three time points (from left to right: pre- to post-treatment, pre-treatment to follow-up and post-treatment to follow-up) against Standard Errors of those effect sizes (se(SMD))

Disclosures

Contributions

TJB and SPY gathered and extracted the data and TJB undertook the analysis and wrote the first draft of the manuscript. JYFL helped in the design of the study and in revising drafts of the manuscript.

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